

REMARKS

Claims 2-4, 16-18, 24, 25, 27, 30, 32, 33 and 35-41 were pending in this application. Claim 33 is now cancelled without prejudice to Applicant's right to prosecute its subject matter in the present application and in related applications. Claims 2, 3 and 30 are amended without any intent of disclaiming equivalents thereof. Accordingly, claims 2-4, 16-18, 24, 25, 27, 30, 32 and 35-41 are pending and presented for consideration.

Claim Amendments

Support for amendments to claim 30 is found in the specification at least, for example, at page 12, lines 31-34, and at page 13, lines 13-21. In addition, claims 2 and 3 are amended to depend from claim 30.

Applicant submits that the amendments to the claims introduce no new matter.

Rejections under 35 U.S.C. § 112, first paragraph, written description, new matter

Claims 2-4, 16-18, 24, 25, 27, 30, 32, 33, 35-41 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Specifically, the Examiner asserts that the specification as originally filed does not provide support for the limitation “. . . so that the substituted Cys may form a disulfide bond with a Cys corresponding to position 29 of human erythropoietin” recited in claim 30. Applicant respectfully disagrees with the Examiner. Applicant submits that the specification as originally filed clearly provides support for the objected-to limitation recited in claim 30. For example, support can be found in the specification on page 13, lines 4-21. The objected-to limitation is therefore not new matter.

However, in order to advance prosecution of the present application, Applicant has amended claim 30 to specifically recite “the EPO portion comprises a Cys at a position corresponding to Trp₈₈ of human erythropoietin and an amino acid other than Cys at a position corresponding to position 33 of human erythropoietin such that the EPO portion comprises a Cys₂₉-Cys₈₈ disulfide bond.” Support for the amendment can be found in the specification at least on page 13, lines 13-21. Therefore, Applicant submits claim 30 as amended fully complies with the written description requirement. Accordingly, Applicant respectfully requests the

rejection of claim 30 and its dependent claims 2-4, 16-18, 24, 25, 27, 32, 33, 35-41 be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph, enablement

Claims 2-4, 16-18, 24, 25, 27, 30, 32, 33, 35-41 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. Specifically, the Examiner asserts that claim 30 is not enabled because it recites that the EPO portion contains “an amino acid other than Cys at a position corresponding to position 33 of human erythropoietin” and “retains erythropoietin activity.” According to the Examiner, prior art reference Boissel *et al.* teaches that when cysteine at position 33 was changed to a proline, the EPO protein had greatly reduced *in vitro* biological activity. Without acquiescing to the rejection, and solely to advance prosecution, Applicant has amended claim 30 to specifically recite “the EPO portion comprises a Cys at a position corresponding to Trp₈₈ of human erythropoietin and an amino acid other than Cys at a position corresponding to position 33 of human erythropoietin such that the EPO portion comprises a Cys₂₉-Cys₈₈ disulfide bond.” Applicant traverses the rejection to the extent it is maintained over the claims as amended.

Applicant submits that, contrary to the Examiner’s assertion, the specification provides a working example (*i.e.*, Example 13) demonstrating that the Fc-EPO fusion protein as claimed in claim 30 retains erythropoietin activity. Specifically, Example 13 discloses an Fc-EPO fusion protein including the EPO portion containing a cysteine at position 88 and a proline at position 33 such that the EPO portion comprises a Cys₂₉-Cys₈₈ disulfide bond (*i.e.*, Fc-EPO (Cys₂₉-Cys₈₈)). Example 13 further discloses that the Fc-EPO (Cys₂₉-Cys₈₈) protein was found to be 1.5- to 2-fold more active than the Fc-EPO (wild-type) protein based on the proliferation assays conducted in TF-1 cells (*see, e.g.*, page 35, lines 18-19).

In addition, Applicant has previously overcome the scope of enablement rejection with respect to the EPO mutations applying the test set forth in *In re Wands*, 858 F.2d 731 (CAFC 1988). As argued in the response filed on July 2, 2004, the specification is sufficient to enable one of ordinary skill in the art to practice the invention without undue experimentation because (1) the specification of the present invention provides adequate guidance or directions on how to generate mutations, (2) there was a high level of skill in the EPO art at the time when the

application was filed, and (3) all of the methods needed to test EPO function were well known in the art. A copy of the response filed on July 2, 2004, is enclosed as Exhibit A for the Examiner's convenience.

Accordingly, Applicant respectfully requests the rejection of claim 30 and its dependent claims be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 2-4 and 30 are rejected under 35 U.S.C. § 112, second paragraph, for being indefinite. Specifically, the Examiner alleges that previously pending claim 30 is indefinite because it is not clear which substituted Cys of positions 86, 87, 88 or 91 may form a disulfide bond with Cys at position 29.

Without acquiescing to the rejection, and solely to advance prosecution, Applicant has amended claim 30 to specifically recite "the EPO portion comprises a Cys at a position corresponding to Trp₈₈ of human erythropoietin and an amino acid other than Cys at a position corresponding to position 33 of human erythropoietin such that the EPO portion comprises a Cys₂₉-Cys₈₈ disulfide bond." Therefore, Applicant respectfully requests the rejection of claim 30 be withdrawn.

The Examiner further asserts that claims 2-4 are indefinite because they depend from a cancelled claim 28. Applicant has amended claims 2-4 to depend from independent claim 30. Accordingly, Applicant respectfully requests the rejection of claims 2-4 be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully submits that pending claims 2-4, 16-18, 24, 25, 27, 30, 32 and 35-41 are in condition for allowance. The Examiner is invited to telephone the undersigned agent to discuss any remaining issues.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Fangh Chen', is written over a horizontal line.

Fangh Chen, Ph.D.
Agent for the Applicants
Kirkpatrick & Lockhart Nicholson
Graham LLP
One Franklin Street
Boston, Massachusetts 02111-2950

Date: April 20, 2006
Reg. No. 51,551

Tel. No.: (617) 261-3198
Fax No.: (617) 261-3175

Customer Number: 022832